

## PATENT COOPERATION TREATY

## PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 27 MAR 2006

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|---|---|--|-----------------------|
| Applicant's or agent's file reference<br>16139/09052  | FOR FURTHER ACTION  |  | See Form PCT/IPEA/416 |
| International application No.<br>PCT/US04/37813   | International filing date (day/month/year)<br>12 November 2004 (12.11.2004) | Priority date (day/month/year)<br>12 November 2003 (12.11.2003)                                      |                       |
| International Patent Classification (IPC) or national classification and IPC<br>IPC: A61K 31/40( 2006.01);C07D 207/34( 2006.01)<br>USPC: 514/423;548/537  |   |  |                       |
| Applicant<br>UNIVERSITY OF SOUTH CAROLINA   |   |  |                       |
| <p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>4</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> |   |  |                       |
| <p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>  |   |  |                       |
| Date of submission of the demand<br>08 June 2005 (08.06.2005)   |   | Date of completion of this report<br>16 March 2006 (16.03.2006)                                      |                       |
| Name and mailing address of the IPEA/ US<br>Mail Stop PCT, Attn: IPEA/US<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, Virginia 22313-1450<br>Facsimile No. (571) 273-3201  |   | Authorized officer<br>Laura L. Stockton, Ph.D. <i>J. Roberts for</i><br>Telephone No. (571) 272-1600 |                       |

Form PCT/IPEA/409 (cover sheet)(April 2005)

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/US04/37813

## Box No. I Basis of the report

1. With regard to the language, this report is based on:

- ☒ the international application in the language in which it was filed.
- ☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
- ☐ publication of the international application (under Rule 12.4(a))
- ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☒ the international application as originally filed/furnished
- ☒ the description:  
pages 1-81 as originally filed/furnished  
pages\* NONE received by this Authority on \_\_\_\_\_  
pages\* NONE received by this Authority on \_\_\_\_\_
- ☒ the claims:  
pages 82-101 as originally filed/furnished  
pages\* NONE as amended (together with any statement) under Article 19  
pages\* NONE received by this Authority on \_\_\_\_\_  
pages\* NONE received by this Authority on \_\_\_\_\_
- ☒ the drawings:  
pages 1-11 as originally filed/furnished  
pages\* NONE received by this Authority on \_\_\_\_\_  
pages\* NONE received by this Authority on \_\_\_\_\_
- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/figs \_\_\_\_\_
- ☐ the sequence listing (*specify*): \_\_\_\_\_
- ☐ any table(s) related to the sequence listing (*specify*): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/US04/37813

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application☒ claims Nos. 36

because:

☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require an international preliminary examination (*specify*):☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 36 are so unclear that no meaningful opinion could be formed (*specify*):

Claim 36 fails to provide a structure or nomenclature of a phosphodiesterase-4 inhibitor or a calcium channel blocker that can be administered to prevent or treat a cardiovascular or a respiratory disorder. Therefore, claim 36 is unsearchable.

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):☐ no international search report has been established for said claims Nos. \_\_\_\_\_☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b) and 13ter.2.☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.☐ See Supplemental Box for further details

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.  
PCT/US04/37813**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. Statement**

|                               |                              |     |
|-------------------------------|------------------------------|-----|
| Novelty (N)                   | Claims <u>1-35 and 37-43</u> | YES |
|                               | Claims <u>NONE</u>           | NO  |
| Inventive Step (IS)           | Claims <u>NONE</u>           | YES |
|                               | Claims <u>1-35 and 37-43</u> | NO  |
| Industrial Applicability (IA) | Claims <u>1-35 and 37-43</u> | YES |
|                               | Claims <u>NONE</u>           | NO  |

**2. Citations and Explanations (Rule 70.7)**

Claims 1-35 and 37-43 lack an inventive step under PCT Article 33(3) as being obvious over Johnson et al. (Journal of Pharmaceutical Sciences (1979), 68(8), pages 955-958).

Applicant claims pyrrole compounds. Johnson et al. teach pyrrole compounds that are structurally similar to the instant claimed compounds. See, for example, the compounds in the table at the bottom of page 955. The difference between the compounds of Johnson et al. and the compounds instantly claimed is that of hydrogen versus a methyl (e.g., homologues).

To those skilled in chemical art, one homologue is not such an advance over adjacent member of series as requires invention because chemists knowing properties of one member of series would in general know what to expect in adjacent members. The instant claimed compounds would have been obvious because one skilled in the art would have been motivated to prepare homologs of the compounds taught in Johnson et al. with the expectation of obtaining compounds which could be useful in the pharmaceutical arts. The instant claimed compounds would have been suggested to one skilled in the art and therefore, lack an inventive step.

Claims 1-35 and 37-43 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.